REMARKS

Claims 14-17 are pending and are rejected under 35 U.S.C. § 103. Applicants address each basis for rejection as follows.

Claim Amendments

Claims 14 and 15 have been amended to recite that the thorium-227 "is chelated by a bifunctional chelator" and "is not attached to a phosphate group or a bone targeting group." Support for this amendment is found, for example, at page 23, lines 4-5, and page 24, lines 7-9, of the specification as filed. No new matter has been added by the present amendments.

Applicants reserve the right to pursue any cancelled subject matter in this or in a continuing application.

Rejection under 35 U.S.C. § 103

Claims 14-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Larsen et al. (US 2001/00086625A1; "Larsen '625") in view of Larsen et al. (WO 02/05859A2; "Larsen '859"). In particular, the Office states (page 3):

> The thorium-227 of Larsen '625 encompasses the thorium-227 of the instant claims and is capable of the same functions, such as being suitable for targeting to soft tissues and has the same properties.

And the Office further states (page 4):

> The reference of Larsen et al. '859 was used to teach of the dosage range for thorium-227 wherein the thorium-227-chelator complex for administration may be in a pharmacologically acceptable carrier delivered at doses of 10kBq-2MBq/kg bodyweight for use in therapy and/or palliation related to malignant diseases affecting bones **and/or soft tissue**. (Emphasis original.)

Applicants respectfully submit that the claims as amended are free of the present obviousness rejection.

Larsen '625 describes receptor binding conjugates which are directed to or against tumors expressing a folate binding protein. These conjugates include an antibody, a radionuclide, and a folate, where the radionuclide is bound through the use of a bifunctional chelator with coupling reactivity towards certain groups on the proteins (see paragraph [0020]). As the Office notes, the replacement of the folate with another receptor binding molecule, such as estrogen or testosterone, is postulated. Larsen '615, however, provides no teaching as to the types of chelators that could be used in the presently claimed complexes and, in the examples, only describes use of 1-ethyl-3-(3-dimethylaminopropyl)carbondiimide, which was used to activate folic acid for coupling to the human IgG antibody (see paragraph [0046]). Clearly, because folate is used to target the complex to tumors, this is not a teaching or suggestion of conjugating thorium-227 and a targeting moiety by chelating with a bifunctional chelator where the thorium-227 is not attached to a phosphate group or bone targeting group. As such, the Larsen '625 reference fails to teach or suggest this element of the claimed invention.

Larsen '859 describes the use of thorium for the treatment of calcified tumors, bone tumors, bones, and bone surfaces. Applicants submit that the conjugates described in Larsen '859 are only described in combination with bone-targeting moieties, in particular, phosphonates. On this point, Applicants direct the Office's attention to page 4, lines 17-33 of Larsen '859, where the reference describes thorium in complexes characterized as being chelated by *an agent that targets the complex to the bone*, such as phosphonates. In particular, here Larsen '859 exemplifies DOTMP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetramethylenephosphonic acid) and DTMP (diethylenetriamine-N-N',N''-pentamethylene-phosphonic acid) as complexing agents that serve to target the complex to bone. Bifunctional chelators which do not contain bone targeting groups are not described in Larsen '859. The claims as amended require that the thorium-227 to be chelated by a bifunctional chelator and not be attached to a phosphate group or bone targeting group. The Larsen '859 reference, like the Larsen

'625 reference, fails to teach or suggest this element of the claimed invention.

In short, neither Larsen '625 nor Larsen '859 describes a complex containing thorium-227 and a targeting moiety where the thorium-227 is chelated by a bifunctional chelator and is not attached to a phosphate or bone targeting group. Neither of the cited documents, alone or in combination, teaches or suggests all of the features of the claimed invention and, therefore, cannot render the presently claimed invention obvious. The obviousness rejection over the combination of Larsen '625 and Larsen '859 should be withdrawn.

CONCLUSION

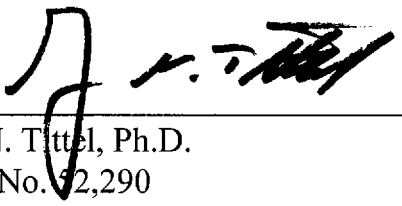
Applicants submit that the application is now in condition for allowance, and such action is hereby respectfully requested.

Enclosed is a Petition to extend the period for replying to the final Office Action for three (3) months, to and including October 29, 2010, and an authorization to charge the required extension fee to Deposit Account No. 03-2095.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 29 October 2010



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